Abstract

We report a young patient who developed a stiff man syndrome (SMS) long after remission of Hodgkin lymphoma. This patient is remarkable because he has had several other potentially autoimmune or paraneoplastic neurological syndromes including limbic encephalitis and demyelinating polyneuropathy which also occurred years after remission from Hodgkin disease.

Key words: Stiff man syndrome; chronic inflammatory demyelinating polyneuropathy; Hodgkin lymphoma; limbic encephalitis; paraneoplastic syndrome; Guillain-Barré syndrome.

Introduction

Hodgkin lymphoma is sometimes associated with neurological paraneoplastic diseases. In general, paraneoplastic neurological syndromes parallel the course or are the presenting sign of an underlying neoplasm (Voltz et al., 2002; Dropcho et al., 1998). Rarely these syndromes develop years after remission from Hodgkin disease. Hammack et al., however, reported six cases of paraneoplastic cerebellar degeneration one to 54 months after remission form Hodgkin disease (Hammack et al., 1992). We present a patient who is remarkable because of the combination of several autoimmune or paraneoplastic neurological syndromes emerging long after total remission of Hodgkin disease. He consecutively developed an episode of limbic encephalitis, demyelinating polyneuropathy and stiff man syndrome (SMS). The development of these syndromes during remission of Hodgkin lymphoma has not been reported yet.

Case report

A 38-year-old man of Indian origin is known with non insulin dependent diabetes mellitus since 1997. In 1998, he presents with a swollen inguinal lymph node, night sweats, fever of unknown origin and fatigue. Hodgkin lymphoma grade IIB is diagnosed with involvement of inguinal and pelvic lymph nodes. He is treated with an adriamycin, bleomycin, vinblastine, dacarbazine (ABVD) regi-
paraneoplastic syndromes after remission of neoplastic disease is a rare observation. Limbic encephalitis is a paraneoplastic neurological syndrome often associated with small cell lung carcinoma (50%), testicular (20%), breast (8%) and other tumors (Gultekin et al., 2000). Limbic encephalitis has been described earlier in association with Hodgkin disease (Bernard et al., 2003). Limbic encephalitis causes short-term memory loss, confusion and behavioural changes, but seizures can also occur. CSF often contains elevated protein combined with mild mononuclear pleocytosis. Sometimes oligoclonal bands can be detected in CSF (Gultekin et al., 2000; Vincent et al., 2004). MRI scan usually shows hyperintense T2 lesions in both amygdala and hippocampus. These lesions in the temporal lobe happen to be transient during the course of the disease (Dirr et al., 1990). Our patient did have T2 lesions at the anterior temporal lobe, but these lesions disappeared during follow-up MRI. Thyroid function should be analysed to rule out the possibility of Hashimoto encephalopathy, a condition also characterised by seizures, stupor and psychosis (Ferracci et al., 2003). Recently the presence of voltage-gated potassium channel (VGKC) antibodies was demonstrated in some cases of limbic encephalitis. These antibodies do not discriminate between idiopathic or paraneoplastic limbic encephalitis but probably indicate a good response to immunotherapy (Pozo-Rosich et al., 2003; Vincent et al., 2004). No residual anti-VGKC antibodies could be detected in 2004 (courtesy Prof. A. Vincent, Oxford University, UK). The five year delay between the limbic encephalitis manifestations and the test could be the reason for the negative results.

Peripheral nervous system abnormalities occur in five percent of patients with lymphoma (Hughes et al., 1994; Mallecourt et al., 2000). Demyelinating polyneuropathies such as Guillain-Barré syndrome and CIDP have been reported in association with lymphoma (Maslovsky et al., 2001). Our patient developed a demyelinating neuropathy that is best classified as CIDP. Vinca alkaloids such as vinblastine are the only drugs used in lymphoma which commonly cause neuropathy of the sensorimotor axonal type (Hughes et al., 1994).

Stiff man syndrome is characterised by muscular rigidity and spasms of predominantly axial and proximal limb muscles. Emotional or audiovisual stimuli can elicit spasms of the legs and trunk. Stiffness and spasms fluctuate throughout the day and lessen or even disappear during sleep or narcosis (Meinck et al., 2002). An autoimmune pathogenesis is suspected. About 70 percent of all patients have serum and CSF anti-GAD65 antibodies (Dalakas et al., 2001). GABA is one of the most important inhibitory neurotransmitters in the brain and spinal cord. Anti-GAD65 antibodies are an excellent marker for SPS, but following their titers has no value in monitoring the disease nor is there a relationship between the antibody titer and disease severity (Rakocevic et al., 2004). Given the history of Hodgkin lymphoma and the presence of anti-GAD65 antibodies, the SMS in our patient may be an auto-immune complication of the lymphoma. SMS rarely has a paraneoplastic etiology. If so, the tumour most commonly involved is breast cancer in association with anti-amphiphysine antibodies (Bataller et al., 2003). Serum analysis in 2004 showed no anti-amphiphysine antibodies. This patient developed a SMS 4 years after remission of the lymphoma while paraneoplastic syndromes normally parallel the course of a malignancy or are the presenting sign of an occult cancer. Intravenous immunoglobulins have been successful in some cases (Dalakas et al., 2001). Our patient responds only partially to the IVIg therapy with diminished abdominal spasms and improved gait.

In conclusion, this case demonstrates that Hodgkin disease can cause multiple delayed neurological syndromes long after remission of the lymphoma.

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